

LISTING AND AMENDMENT OF THE CLAIMS

1-25. (Canceled).

26. (Currently Amended) A method for investigating a body fluid ~~determining whether disseminated cancer cells are present in a blood sample from a human subject having or suspected of having cancer for disseminated cancer cells, which, wherein the method~~ comprises:

~~—obtaining a cell-containing fraction from the body fluid with enrichment of cancer cells and determining in the cell-containing fraction the expression of at least 2 genes which are selected from the group consisting of~~

~~i) a human-manganese-superoxide-dismutase gene;~~

~~ii) a human-thioredoxin-reductase-1 gene; and~~

~~iii) a human-glutathione-peroxidase-1 gene;~~

~~—providing a further cell-containing fraction of the body fluid from the same individual and determining the expression of the genes in the further cell-containing fraction; and~~

~~—comparing the expression for each of said at least 2 genes in the cell-containing fraction with its expression in the further cell-containing fraction, and~~

(a) obtaining a blood sample from a human subject having or suspected of having cancer, collecting from the blood sample a cell fraction that comprises mononuclear cells (MNC fraction), removing a fraction of the MNC fraction to obtain test fraction A', passing the remaining MNC fraction through a screen with a mesh or pore width of 17-27 μm , and collecting cells from the screen to obtain test fraction C;

(b) isolating mRNA from test fraction A' and test fraction C to obtain mRNA samples;

(c) measuring in each of the mRNA samples obtained in step (b) the expression level of manganese superoxide dismutase (MNSOD) mRNA that encodes a protein having the amino acid sequence of SEQ ID NO:13 or an allelic variant thereof, thioredoxin reductase (TXNRD1) mRNA that encodes a protein having the amino acid sequence of SEQ ID NO:15 or an allelic variant thereof, and glutathione peroxidase (GPX1) mRNA that encodes a protein having the amino acid sequence of SEQ ID NO:17 or an allelic variant thereof, wherein said measuring is by reverse transcription into cDNA and PCR;

(d) determining the expression ratio of MNSOD, TXNRD1, and GPX1 from test fraction C to test fraction A'; and

(e) comparing the expression ratio for each of MNSOD, TXNRD1, and GPX1 determined in step (d) to a control limit for expression for each of MNSOD, TXNRD1, and GPX1 in blood samples of healthy human subjects,

and wherein the body fluid is selected from blood and bone marrow and an elevated expression of at least one of said at least 2 genes determined in the cell-containing fraction, as compared to its expression in the further cell-containing fraction, an expression ratio determined in step (d) higher than the control limit of expression of at least one of MNSOD, TXNRD1 and GPX1 indicates the presence of disseminated cancer cells in the body fluid blood sample from a human subject having or suspected of having cancer.

27-31. (Canceled).

32. (Currently Amended) The method ~~as claimed in~~ claim 26, wherein the ~~elevated expression of at least one of said genes~~ presence of disseminated cancer cells in the blood sample from a human subject having or suspected of having cancer indicates the presence of a tumor.

33. (Canceled).

34. (Currently Amended) The method ~~as claimed in~~ claim 26, wherein the ~~elevated expression of at least one of said genes~~ presence of disseminated cancer cells in the blood sample from a human subject having or suspected of having cancer indicates a risk to develop a metastasis or a recurrence.

35-45. (Canceled).

46. (Currently Amended) The method ~~as claimed in~~ claim 29 ~~26~~, wherein the screen has a mesh or pore width of about 20 μm .

47-70. (Canceled).

71. (New) The method of claim 26, wherein the cDNA obtained by reverse transcription comprises the nucleotide sequences of SEQ ID NO:1 and 2 for MNSOD mRNA; SEQ ID NO:4 and 5 for TXNRD1 mRNA, and SEQ ID NO:7 and 8 for GPX1 mRNA.

72. (New) The method of claim 71, wherein the control limit for expression has been determined by performing the following steps:

(f) obtaining blood samples from healthy human subjects not suffering from cancer, collecting a cell fraction that comprises mononuclear cells (MNC fraction) from the blood samples, removing a fraction of the MNC fraction to obtain reference fraction A', passing the remaining MNC fraction through a screen with a mesh or pore width of 17-27 μ m mesh, and collecting cells from the screen to obtain reference fraction C;

(g) optionally isolating CD45-positive lymphocytes from reference fraction A' to obtain reference fraction A,

(h) isolating mRNA from reference fraction A' or A and reference fraction C to obtain mRNA samples;

(i) measuring in each of the mRNA samples obtained in step (h) the expression level of MNSOD mRNA that encodes a protein having the amino acid sequence of SEQ ID NO:13 or an allelic variant thereof, TXNRD1 mRNA that encodes a protein having the amino acid sequence of SEQ ID NO:15 or an allelic variant thereof, and GPX1 mRNA that encodes a protein having the amino acid sequence of SEQ ID NO:17 or an allelic variant thereof, wherein said measuring is by reverse transcription into cDNA and PCR; and

(j) determining the average for the expression ratio of MNSOD, TXNRD1, and GPX1 from reference fraction C to reference fraction A' or A, and determining a control limit for expression.

73. (New) The method of claim 71, wherein the control limit for expression has been determined by performing the following steps:

(f) obtaining blood samples from healthy human subjects not suffering from cancer, collecting a cell fraction that comprises mononuclear cells (MNC fraction) from the blood samples, removing a fraction of the MNC fraction to obtain reference fraction A', passing the remaining MNC fraction through a screen with a mesh or pore width of 17-27 μm mesh, and collecting cells from the screen to obtain reference fraction C;

(g) isolating CD45-positive lymphocytes from reference fraction A' to obtain reference fraction A,

(h) isolating mRNA from reference fraction A and reference fraction C to obtain mRNA samples;

(i) measuring in each of the mRNA samples obtained in step (h) the expression level of MNSOD mRNA that encodes a protein having the amino acid sequence of SEQ ID NO:13 or an allelic variant thereof, TXNRD1 mRNA that encodes a protein having the amino acid sequence of SEQ ID NO:15 or an allelic variant thereof, and GPX1 mRNA that encodes a protein having the amino acid sequence of SEQ ID NO:17 or an allelic variant thereof, wherein said measuring is by reverse transcription into cDNA and PCR; and

(j) determining the average and standard deviation for the expression ratio of MNSOD, TXNRD1, and GPX1 from reference fraction C to reference fraction A, and determining a control limit for expression.